WHAT IS '*SCHISTOSOMUM MANSONI*' SAMBON 1907?

BY

DR. A. LOOSS,

PROFESSOR OF PARASITOLOGY, SCHOOL OF MEDICINE, CAIRO

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About a year ago Dr. SAMBON, of the London School of Tropical Medicine, startled the scientific world interested in human parasitology by the creation of a new species of blood fluke, *Schistosomum mansoni*, which he stated had hitherto been confounded with *Sch. hæmatobium* (1907a, p. 117). A suggestion to this effect had been made as far back as 1903 by Sir PATRICK MANSON. SAMBON's new species was thus readily adopted by MANSON in the new edition of his 'Tropical Diseases' (1907, p. 660). From the West Indies there had come information which seemed to corroborate Dr. SAMBON's views (HOLCOMB, 1907). Later, the author gave a somewhat fuller account of the new species (1907b, p. 303), and quite recently, he mentioned its existence as a fact in a paper 'On the Part played by Metazoan Parasites in Tropical Pathology,' read before the Society of Tropical Medicine and Hygiene, London (1908, p. 29f). In this paper and in the ensuing discussion repeated allusion was made to the views hitherto held with regard to Bilharzia and Bilharziosis by the workers in Egypt in general, and particularly by myself. It was hinted that we had not recognised the differences between two easily distinguishable species. If Dr. SAMBON's view were correct, all of us who have devoted attention to the subject, would have indeed been wandering in the dark since the time of BILHARZ himself, fifty-seven years ago. Since such a charge has practically been made I feel it necessary to take up the defence. I may as well at once say that when in London two years ago I dropped some well-meant hints of warning to be cautious, whether to Sir PATRICK MANSON or to Dr. SAMBON I do not remember. I am sorry that these hints have not been heeded, for if so the present disagreeable discussion might not have become necessary.

Being at present fully occupied with some other work I must limit myself to the discussion of some points of primary importance; but it is possible that I may take an early opportunity of returning to the subject in more detail. Speaking quite generally, I may say even now that those of us who have seen anything of Bilharziosis in Egypt are convinced that the scientific problem it offers is more complicated than Dr. SAMBON seems to imagine; it is a problem which will require a long and close collaboration of the Anatomist, the Pathologist, and the Helminthologist before it may be considered as solved in every detail. There is, further, one thing which can not be too strongly emphasised at the very outset, and this is that any theory, be it ever so cleverly based on the biology of the parasite, must be wrong if it contradicts the facts supplied by the Anatomist and the Pathologist; and also that any other theory, however plausible its explanation of the anatomo-pathological observations, can not represent the truth so long as it is irreconcilable in any detail with the biology of the parasite. I may mention in passing that several theories recently brought forward as explanations of the aetiology of certain human diseases caused by worms are open to the latter objection; the theory of SAMBON is the latest of these, and a very interesting one it is, not perhaps so much for the arguments by which, but on account of the manner in which it is supported.

In order to make the purport of what I have to say hereafter quite clear, I will state that I do not consider it my task to prove whether or no there exists a *Schistosomum mansoni*. Among scientific workers it is a good custom that anyone who believes he has made a new discovery also takes the trouble to prove it; it is not customary among scientists to assert something and call for the help of others to establish it. In the case which I am about to discuss, it is Dr. SAMBON who, acting upon a suggestion of Sir PATRICK MANSON, formally published *Schistosomum mansoni* as a new species. After the usage generally adopted in science, the merit of the discovery is his when the discovery is right. But with him also must rest the responsibility of bringing forward all the evidence which may be reasonably demanded in support of it. Dr. SAMBON, indeed, supports his action by a certain amount of evidence; but he is obviously aware himself that, especially, its zoological part (i.e. the possibility of distinguishing the adult forms) is practically nil. He therefore concludes his answer to the various objections made in the discussion by expressing the hope (in a form, by the way, which I fail to appreciate) that I would soon be able to provide that description of the adult forms which he himself was unable to produce (p. 46). I am sorry that I cannot accept the part thus assigned to me. If Dr. SAMBON had not sufficient material to demonstrate beyond doubt the specific independence of *Sch. mansoni*, he might with advantage have postponed the publication of the name until such necessary material was available. Since he has gone so far as to publish the name, and thereby implicitly claims to have made an important discovery, I think that it is incumbent upon him, and not upon me (or any other), to do the work of supplying such proof as the rest of the scientific world may ask. As I have already said, I cannot consider it as my legitimate task to prove or disprove the existence of a '*Sch. mansoni*.' What I propose to do is to point out the inadequacies of Dr. SAMBON's theory. Doing this, i.e., giving the reasons a g a i n s t SAMBON's theory, amounts to practically the same thing as giving the reasons f o r the views held by me with regard to some fundamental items in the biology of *Sch. hæmatobium*. I am not displeased to have this opportunity: for the rest, every reader is free to form his own judgment.

The reasons which lead Dr. SAMBON to assert the existence of a separate species, '*Sch. mansoni*,' are three: a zoological, a pathological, and a geographical one. The first is afforded 'chiefly' by the ova. 'In *Sch. hæmatobium* the eggs are more or less lanceolate, and provided with a short, straight, terminal spine; in *Sch. bovis* they are spindle-shaped, and provided with a short, terminal, heart-shaped spine; in *Sch. japonicum* they are ovoid, and have no spine; and in *Sch. mansoni* they are oval and provided with a stout, lateral spine' (1908, p. 31). The adults producing the two varieties of eggs are as yet indistinguishable. Dr. SAMBON 'had the opportunity of examining several specimens collected at post mortems in Egypt and Uganda.' He 'noticed that whilst the majority of female worms contained within their uterine tubes the characteristic ova of *Sch. hæmatobium*, with a short terminal spine at the posterior extremity, two presented lateral-spined ova. These had been removed from the gynaecophoric canal of males differing in no appreciable way from those clasping the more common kind.

Unfortunately, the material at hand was so badly preserved that it precluded any study of comparative anatomy' (1907b, p. 303).

The second specific character of *Sch. mansoni* is, according to Dr. SAMBON, given in its 'different anatomical habitat' and its 'specific pathogenic action' (1908, p. 32). '*Sch. mansoni* does not affect the genito-urinary organs, its ova are eliminated solely by way of the intestine; they are never found in the urine. The patients harbouring this parasite suffer from a haemorrhagic enteritis, but they never present haematuria' (1907a, p. 117). The third reason for assuming the existence of a *Schistosomum* different from *Sch. hæmatobium*, is found by Dr. SAMBON in the peculiar geographical distribution of *Sch. mansoni*. According to the data published in literature, the new species is 'probably' alone present in the West Indies, for endemic haematuria is unknown there. The same may be said with regard to the Congo Free State, where careful recent investigations have shown the absence of haematuric bilharziosis and the frequency of a rectal infection, in which the ova of the parasite bear invariably a lateral spine. In the Cape Colony, on the other hand, haematuria is very common; HARLEY, BROCK, and others working in those districts state in their articles on the subject, that they never encountered the egg with the lateral spine. In Egypt, both *Sch. hæmatobium* and *Sch. mansoni* are found side by side, but the former appears to be far more prevalent, and is certainly more in evidence, owing to the haematuria to which it gives rise. That is probably the reason why the two forms have been confounded, and the scarce, laterally-spined ova looked upon as abnormal and distorted (p. 32). SIR PATRICK MANSON, on page 660 of his text-book, shortly states that BILHARZ in 1851 noted the presence of a *Schistosomum* producing lateral-spined eggs, but confounded it with *Sch. hæmatobium*.

We will now analyse these reasons given by Dr. SAMBON somewhat in detail. I begin with the zoological. It is the most important; for the foundation of a new species is, to put it briefly, in the first place a 'zoological act.' In order to establish a new species s a f e l y it is necessary to point out c o n s t a n t l y present and, if possible, e a s i l y recognisable zoological c h a r a c t e r s by which it may be distinguished from related forms. The less constant and the less definite the characters of a presumed new species are, the more it is contestable from the zoological standpoint. The characters themselves must, first and foremost, be derived from the adult stages. With regard to this point, Dr. SAMBON's evidence is nil. He has examined some badly preserved specimens, but the males showed no difference at all from those of *Sch. hæmatobium*, and the females differed in the shape of the egg only. To this latter we shall return later; speaking of the adults, I may state, from a general point of view, that I would not, *a priori*, consider it as a serious objection to Dr. SAMBON's views if there really were no marked anatomical differences between the adults of the supposed two species. There are some few cases known in which certain forms resemble each other to such an extent that they might well be representatives of the same species, did not other factors—such as they are known to us at present—seemingly exclude the possibility of the forms being the same thing. Dr. SAMBON, in order to make the absence of all distinctive characters of his new species appear less weighty, dwells at some length on two cases in which, after a long and tedious comparison of many adult specimens, I have myself come to similar conclusions. It would lead me too far to discuss these cases in detail here. I will only remark that one of them has no bearing on the case at present under discussion, inasmuch as the forms in question show differences which, though slight, are yet sufficiently pronounced to enable any expert to distinguish the respective forms as easily as he may distinguish *Sch. hæmatobium* and *Sch. bovis*. In the second case, a parasite was found to inhabit several mammals, but to be entirely absent from birds, in Europe; whereas a similar form, in North Africa, could never be found in the same mammals, but was present in birds which never visit Europe. In this case, I of course depend upon the facts available at present, and it is very probable that a comparison of a larger supply of new material (my own investigations were made 15 years ago) will reveal structural differences here also. But unless the difference be cleared up by new observations I feel compelled to consider the respective forms as different, in spite of their apparent structural identity. However, Dr. SAMBON, or anybody else, is fully at liberty to show that the premises on which my opinion is based are erroneous. If he succeeds in showing this by irrefutable facts I shall certainly be the first to change my opinion.

But, before doing so, I want to hear facts, just as in the present article I am about to point out a number of facts which are irreconcilable with Dr. SAMBON'S theory. He assures his audience that 'certainly there were more and better reasons to separate *Sch. mansoni* from *Sch. hæmatobium*' (1908b, p. 46) than there were in my two cases referred to by him. We shall see how far this is true.

Dr. SAMBON first pretends that the other known *Schistosoma* species do not show any marked differences in their adult stages. 'The *Sch. bovis*, for instance, resembles the *Sch. hæmatobium* so closely that, indeed, it would be very difficult for anyone to point out any marked difference between the adult forms of the cattle parasite and those of *Sch. hæmatobium*' (1908b, p. 46). To this I have to reply that Dr. SAMBON is mistaken. To 'anyone' who actually has some helminthological knowledge a single glance with the naked eye will suffice to tell *Sch. hæmatobium* from *Sch. bovis*, and a good pocket lens will suffice to differentiate *Sch. japonicum* from *Sch. hæmatobium*. There are, in addition, quite well-marked internal differences which Dr. SAMBON might have known had he consulted the latest description given of *Sch. bovis* by Leuckart (1894, p. 470f), or the short review I gave of KATSURADA'S paper on *Sch. japonicum* (1905a). The fact that Dr. SAMBON is not apparently aware of the existence of these differences is in itself a poor reason for the statement to his audience that they are really absent. As a matter of fact, in no case does the differentiation of any of the species of *Schistosomum* hitherto described, whether affecting man or animals, depend on the form of the egg alone. Since the various Schistosomes affecting animals are not mentioned by Dr. SAMBON, I will not refer to them any further in this discussion.

Thus, Dr. SAMBON is not able to produce any distinctive anatomical character of the adult *Sch. mansoni*. There remains only the egg. It is a well-known fact that many, but by no means all, species of parasites may be recognised from their eggs. If this is the case, the aspect of the egg is one of the distinctive characters of certain species. I do not, however, at present remember one single case in which two species of parasitic worms acknowledged as independent differed solely by their eggs. The fact is easily comprehensible. If I cannot tell whether two specimens I have before me are individuals of one species or individuals of two species, I cannot tell either whether slight differences I observe in their eggs are specific characters or not. If I so desire, I may assert that there are two species; but, in that case, others will certainly demand proofs of such a statement. Dr. SAMBON pretends that the two shapes of the egg found in association with *Sch. hæmatobium* belong to two different species, but I cannot see that he can possibly prove this zoologically without finding distinctive differences between the adults. For the proof must consist in showing that one form of egg is constantly connected with a certain anatomical structure, and the other form as constantly connected with another anatomical structure of the adults. Until this is done I am afraid that *Sch. mansoni* will find little approval with zoologists, in spite of Dr. SAMBON's contention that 'to zoologists the characters of the ovum should suffice for the determination of a new species' (1908a, p. 31).

The remarkable difference in the position of the spine of the egg of *Sch. hæmatobium* has long attracted the attention of observers, the majority of whom considered the egg with the end spine as the normal, and that with the side spine as abnormal. Various attempts have been made to explain the formation of the latter. Dr. SAMBON refers to these theories, but in a rather peculiar manner. He particularly mentions FRITSCH, 'who had described certain differences in the genital tract of the female, but was under the impression that the females containing the lateral-spined ova belonged to the same species as those containing terminal-spined ova. He therefore explained the difference by abnormality. FRITSCH's explanation was obviously wrong, but his description was perfectly correct' (1908b, p. 46). I should like to know in what way Dr. SAMBON has obtained the evidence for the concluding part of this statement. He has said that the two females he had an opportunity of examining were so badly preserved that any study of their anatomy was precluded. How, then, does Dr. SAMBON know that FRITSCH's description was 'perfectly correct'? I doubt whether he has at all read that author's original article (it is, unfortunately, not accessible to me at present); he has certainly not read the later descriptions of LORTET and VIALLETON, LEUCKART and myself, in the latter two of which FRITSCH's statements with regard to the point under discussion are refuted as incorrect.

I will not tire the reader by a long anatomical description of the structures at issue; suffice it to state that up to this day I have personally found only o n e type in the structure of the internal genital organs of the female, although the uterus may contain in one specimen ova with a terminal, and in a n o t h e r specimen ova with a lateral spine. The position of the spine does not depend upon a preformed difference in the internal structure (which, of course, changes its shape somewhat with the contractions of the body), but on the relative position of the egg during the process of its formation in the ootype. I have tried to show this in a diagrammatic drawing which has recently been copied in various books on Bilharziosis; I may mention in passing that in this figure the lateral-spined egg is placed unusually steep; I have in the meantime come across worms in which the axis of the egg lay almost at right angles to the axis of the ootype. Dr. SAMBON ignores the existence of this drawing as well as the descriptions of LEUCKART and myself; I should like to submit that he will have to account for them if he wants to maintain *Sch. mansoni* as an independent species.

On the whole, the zoological characters of the new species are as vague as they can possibly be. Dr. SAMBON is himself aware of that and refers to a case where, in one instance, ornithologists have based a new species solely upon the character of the egg. I am not in a position to criticise the actions of ornithologists; but the fact that they find something justified is for me not in itself a reason to consider the same thing as justifiable also in helminthology. I would mention, by the way, that the new species of bird will certainly not be generally accepted unless it can be shown that the aberrant shape of the egg is reasonably c o n s t a n t.

The details thus far mentioned are in the main of a technical zoological nature. I should not have been compelled to enter upon them had not Dr. SAMBON tried to show that the foundation of *Sch. mansoni* was justifiable from the zoological standpoint. That it cannot be, will become obvious even to the non-specialist by another fact not mentioned by Dr. SAMBON. The fact is that i n E g y p t t h e e g g s o f *S c h. h æ m a t o b i u m* a n d '*S c h. m a n s o n i*' m a y o c c u r i n o n e a n d t h e s a m e i n d i v i d u a l f e m a l e. This observation is now 57 years old and might have been known to Dr. SAMBON, had he studied the papers of those authors whom he accuses of having failed to recognise an obvious fact. The observation is due to BILHARZ. It is true that BILHARZ did not yet know how to interpret those bodies which we now describe as lateral-spined eggs; but this is of no importance as compared with the fact, that once he found one of these enigmatical bodies in the anterior part of the uterus of a female, the posterior part of which was filled with the ordinary ova. That there was no mistake possible may be gathered from the circumstance that BILHARZ, on a later occasion, and after having discovered the same bodies in the tissues of the liver and the rectum, emphatically repeats that 'such a body was, though once only, but quite undoubtedly, found in the uterus of a female worm, the posterior part of which contained the normal ova' (BILHARZ, 1852, pp. 74 and 75). Besides, BILHARZ has proved too careful an observer to admit of any mistake on his part; as a matter of fact, many a recent 'discovery' with regard to Bilharzia and Bilharziosis may be found described in his paper when one takes the trouble to read it.

If my memory does not quite fail me, I have in the course of years, myself seen several similar females; but considering the occurrence of both shapes of eggs in the same individual as anything but new, and not foreseeing either the importance the specimens would one day gain, I have not separated them from the rest, and it is quite possible that one or the other may be found in the material which I have sent away from here to various places. I very much regret that at the present moment I cannot produce a specimen. It is a curious fact, of which we shall have to speak again later, that the portal veins very often contain only males; the worms within recent years found at the post mortems in the Kasr el Aini Hospital, and kindly left to me by Dr. FERGUSON, were almost exclusively males; in one of the last cases, e.g., there were 64 males but not a single female. I have, however, no doubt that sooner or later I shall be able to establish the accuracy of BILHARZ's observation by the production of an actual specimen.

The occurrence of terminal-spined and lateral-spined eggs in one and the same individual worm is one of the fundamental facts on which my views rest; I wonder how Dr. SAMBON will explain it by his theory.

I have said above that, a priori, a great structural similarity of the adult stages would not necessarily be a proof of there being only one species. If, on the other hand, I am asked to acknowledge a specific difference between *Sch. hæmatobium* and *Sch. mansoni*, in spite of their great internal resemblance, I certainly expect that the other proofs in favour of the existence of a separate species will be absolutely clear and stringent. We will now see how these parts of Dr. SAMBON's evidence stand an earnest scientific test.

There are numerous cases where closely allied parasites (of man or animals) show marked differences with regard to their special habitat in the body of their host; the lesions they produce will then show a peculiar localisation. Closely allied species may further differ in their geographical distribution which is indicated by the geographical occurrence of the respective lesions. It is, therefore, a priori, imaginable that the localisation and the geographical occurrence of certain symptoms may in certain cases be a valuable support for the distinction of the species which cause them. A different question is whether variations observed in the localisation and the geographical distribution of certain symptoms may be used as proof that they are due to different species of parasites. In this connection I must point out that, quite generally speaking, observations of the alleged sort are, in principle, statistical. I do not underestimate the value which statistical observations may have under various circumstances; but it is a fact also that from the same statistics more or less opposite conclusions may be drawn according to the point of view from which they are looked at. I may add that the statistics themselves are by no means all of them equally reliable. On the whole, therefore, I think that it will always be wise to test statistical observations very carefully before considering what they seem to show, as an objective proof of some theory. An excellent example of the truth of what has just been said will be discussed towards the end of this article.

In the case which at present occupies us Dr. SAMBON uses statistical observations referring to the localisation and geographical distribution of certain lesions as additional proofs of the existence of a species of parasite which is zoologically utterly doubtful. Judging a priori, I would consider the species as established, notwithstanding, when the additional proofs were binding and did not leave any visible gap. I am sorry to say that, from my point of view, Dr. SAMBON's proofs do not answer this description.

The second difference between *Sch. hæmatobium* and *Sch. mansoni* is said to be given in the different anatomical habitat, and the specific pathogenic action of the latter form. We will start with the well-established clinical fact that terminal-spined ova alone are voided from the bladder, whereas, lateral-spined are met with in the faeces. The conclusion generally drawn from this observation, and also brought forward in the discussion above mentioned by Sir PATRICK MANSON, is that the lesions of the bladder are caused by worms producing terminal-spined ova, whilst the almost identical lesions of the rectum are caused by worms producing lateral-spined ova; in other words, that the last-named ova appearing in the faeces are derived from the rectal lesions. In connection with this point, Sir PATRICK MANSON asked whether anybody had ever seen a lateral-spined egg in the urine. Nobody could answer in the affirmative; indeed, I do not remember myself to have specially noticed a lateral-spined egg in the urine. Thus far, observations agree very well; however, what I should like to point out is that even if I, or anyone else, had seen a lateral-spined egg in the urine, I would be unable to consider this as a fact of fundamental importance. To me it would appear as an accidental exception, due to accidental reasons, to the rule that the urine contains terminal-spined eggs only. One may examine the faeces of a thousand people without finding an apple-maggot, and in the faeces of the thousand and first there is one; the former observations show that maggots are not a normal appearance in human faeces; the latter observation does not at once demonstrate the contrary, but only shows that it is an occasional exception, the chief interest of which would lie in the question as to the conditions under which the exception occurs. As I have said, I would look at it from this point of view, should a lateral-spined egg some time be found in the urine.

Passing to the supposed causal connection of the lateral-spined ova with the rectal lesions, I must confess that up to a few years past I shared the opinion that the former were derived from the latter. I must state to-day that this was a mistake; in many cases the lateral-spined eggs do not come from the rectal lesions. Desiring, some years ago, to make a drawing of a lateral-spined ovum, and having no faecal material at my disposal I took a papilloma of a preserved rectum and examined for ova. There were plenty of terminal-spined, but not a single lateral-spined could be discovered. New preparations made from other papillomata of the same rectum, gave no better results. Serial sections made of other recta showed similar conditions, in so far as sometimes terminal-spined eggs alone were found, sometimes both forms mixed. In no case, however, have I so far found, in the rectal wall, the lateral-spined eggs quite alone. The point most important in the present connection is that these observations leave no doubt that the vesical and rectal lesions so similar to each other in external appearance also contain one form of egg only. After the theory of Dr. SAMBON, this form is distinctive of *Sch hæmatobium*. *Sch. hæmatobium* is, therefore, capable of producing rectal as well as vesical lesions; I see no reason why, under peculiar circumstances, it should not be able to produce, in one case, vesical lesions alone, and, in another case, rectal lesions alone. The question as to what these peculiar circumstances may be is certainly of great interest, but it is secondary to the fact that both forms of lesions may be produced by *Sch. hæmatobium*. '*Sch. mansoni*' is said by Dr. SAMBON to have 'a specific pathogenic action'; since *Sch. hæmatobium* may produce identical lesions the alleged specificity does not exist, or shows, at least, a very remarkable flaw.

We now come to a more important point. If lateral-spined ova do not occur at all, or occur in insignificant numbers only, in the rectal lesions it is impossible that such ova when they appear in the faeces can be derived from the rectal lesions. I had, in a number of cases selected entirely at random, found no trace of lateral-spined ova in the rectal papillomata; where, then, could the lateral-spined ova come from? Before advancing further I must mention several facts which, in addition to the occurrence of both shapes of eggs in one and the same individual, figure as arguments in my theory as to the nature and the significance of the lateral-spined eggs.

The place where the Bilharzia worms are, in post mortems, usually looked for, and most easily found, is the portal system. I have, since

1893, seen a good many of them; a fact which struck me from the beginning was their very different size. In certain cases, they presented about their normal dimensions; in others, they were markedly smaller, and in some, they hardly reached a third of their normal length. Another fact which sometimes very forcibly obtruded itself to the eye was that the specimens present in an individual case were, among themselves, of very much the same size, i.e., of about the same age. I still possess in my collection the material from one case, which consists, after specimens have been given away, and others have been used for examination, of 62 males, all varying in length from 3 to 4 mm. according to their somewhat different state of contraction. There are, in addition, females (though in fragments only) which must have measured from 5 to 6 mm. so far as their length is still determinable. I also remember another case in which the worms—males alone—presented two different sizes so distinctly that it was not difficult to separate them into two lots, each, of specimens about equal in size. On microscopical examination, all specimens proved to be sexually immature, and the degree of sexual development coincided about with their size. In many cases males were present alone; where both males and females were found they were still isolated; only in some two or three cases could a coupled pair be detected in the portal veins. The more advanced females contained one or a few ova in their uteri, all of them of the lateral-spined type, some of quite unusual shape. These observations only confirmed what had been seen and described by some former writers.

As a helminthologist I have not limited my investigations to the parasites of man, but have carefully and through many years, studied—anatomically and biologically—the Trematodes parasitic in animals. One result of these studies was that, very generally, Trematodes at the approach of their sexual maturity were found to form abnormally shaped eggs. In some most interesting instances the female genital apparatus was, owing to some malformation, found completely shut off from the male apparatus; there was no possibility for the egg-cells to become fertilized, but, nevertheless, the uterus was filled (in one case packed) with ova, all misshapen. In younger but normal specimens of the same species, the uterus contained more or less numerous normal eggs, but in front, there were, sometimes a few, in other cases more, and in others again, crowds of the same abnormal eggs as had been seen in the specimens with the internal defects. In order to fully understand these statements one must, of course, have some knowledge of the anatomy and biology of the parasitic worms in general. I do not expect the ordinary medical man to have them, nor does he want them; but I strongly recommend studies of the sort to all those who indulge in 'formulating ideas' with reference to helminthological questions. Anyone would be laughed at if he tried to write a tale in a language of which he did not know the alphabet; but I might quote dozens of passages from modern papers on helminthological subjects which leave no doubt that the author did not know the significance of the terms he used.

Putting the facts observed in various species of Trematodes together with what had been seen by some earlier observers and myself in the young Bilharzia worms, I came to the conclusion that the lateral-spined must be abnormal eggs. I added that unimpregnated or isolated females would, perhaps, be 'unable to produce other than such abnormal eggs.' I do not claim that this interpretation is the correct one; but I daresay that it is based on a series of actual facts observed in the nearest natural relatives of the Bilharzia worms; in other words, that it is a quite well-founded 'conclusion from analogy.'

Dr. SAMBON, speaking of this theory of mine, refers to an observation of Dr. LEIPER, in which a terminal-spined egg was seen in an 'immature' female, and concludes that by this observation my theory 'is disposed of.' I cannot help finding that Dr. SAMBON is somewhat hasty in disposing of theories which are in contradiction with his own. I see that my young friend LEIPER states the immature condition of the specimen, but I do not see that he states the absence of spermatozoa in her oviduct. Was the worm, therefore, fertilized, or was it not? I further think that for everyone who will look at the case with an open mind it is clear that there is no mathematical line of demarcation between 'maturity' and 'immaturity.' The eggs are formed in the 'ootype' which is situated at about the middle of the body at the posterior end of the long uterus. In the young females found in the portal vein the eggs are lateral-spined. They are gradually pushed along the uterus till at the end they are expelled by the genital aperture situated behind the ventral sucker. Other eggs may follow the first, but, according to our present knowledge, the number of those present at a time remains limited to 5 or 6. When the female is impregnated the formation of normal eggs begins. At about this period we ought to expect the uterus to show, in its hindmost part, a number of terminal-spined eggs, while the anterior part may still contain one or some lateral-spined ova. Such was the case in the specimen observed by BILHARZ; the analogy it presents to some of the Trematodes described above is complete. Had BILHARZ happened to see the specimen an hour or a day later the last lateral-spined egg would have been laid; the specimen would have been 'mature.' Had he happened to see it a day or a week earlier, no terminal-spined eggs might have been formed yet; the specimen was 'immature.' As he actually saw it it was half 'mature' and half 'immature.' For the moment, therefore, I see no reason why my theory should be annihilated by the one accidental observation of Dr. LEIPER,—admitting even that the egg in question were really terminal-spined, and did not only appear as such because the lateral spine was turned towards, or away from, the observer.

Dr. LEIPER himself says in the discussion (p. 45) that his observation makes him believe 'that the explanation was not correct which relied solely upon immaturity as the cause of the lateral spine.' This is quite right, but I have not pretended either, that immaturity is the sole cause of the lateral spine. Dr. SAMBON, in quoting my theory, makes me say that 'the eggs bearing a terminal (obviously a misprint for "lateral") spine probably represent the product of unfertilized females.' He thus does not notice that there is a slight but very important difference between saying 'lateral-spined eggs are the product of unfertilized females,' and saying, as I really have done, that 'unfertilized females are not capable of producing other than abnormal eggs.' As a matter of fact, several earlier authors have pointed out how fertilized females might, under certain conditions, produce lateral-spined eggs also. These suppositions have up to the present day not been proved as true, but they have not been disproved either, and it is at least not impossible that what those authors surmise may actually happen. At any rate, I have never pretended, and do not pretend, that immaturity is the sole cause of the lateral spine; nor is it impossible that immature females, although producing as a rule, lateral-spined eggs, may not, as an exception, produce one or another terminal-spined egg. Biological processes can never be pressed into a mathematical formula to which there is no possible exception.

Speaking of the significance of these eggs I will provisionally quote the opinion of HOLCOMB, who says (1907, p. 62): 'The West Indian infection proves that the lateral-spined eggs are not the eggs of unfertilized females, and some of my cases, which were under observation for one year or more, show only too well the persistence of the type of egg cannot be attributed only to young females.' Before I can respond to this argument several other points must be discussed: I, therefore, at this place, limit myself to quoting HOLCOMB'S objection, and will return to the point later.

The habitat of the m a t u r e Bilharzia worms are the finer ramifications, in the first place, of the vesical and, in the second place, of the rectal veins. As a logical consequence of my theory, one ought to expect that, t h e r e, they produce terminal-spined eggs only. Observation shows that the lesions actually contain such eggs in enormous numbers, and very often a b s o l u t e l y a l o n e. Some stray lateral-spined eggs found at the one place or the other would not shake this rule. Even when large numbers were found in numerous cases the fact would not prove any specific nature of these eggs unless it were shown, either that unimpregnated females cannot possibly get to the same places, or, that impregnated females cannot under any circumstances form lateral-spined eggs.

The young females living in the portal system produce lateral-spined ova, and successively expel them into the surrounding blood. Since the ova are not by themselves mobile the blood stream will carry them deeper into the liver, where, logically, they must finally become arrested in those vessels whose diameter equals their own. The theory held by me thus leads to the logical consequence that lateral-spined eggs must first and foremost accumulate in the liver. Their frequent and often plentiful occurrence in that organ is a well-known fact; indeed it represents another of the pillars on which my theory rests. According to the general belief (which I share) the worms grown up in the portal system reach their definite habitat in the pelvic organs by active wanderings, the vigorous males carrying the weaker females with them in the gynaecophoric canal. It is, however, possible that the females are capable also of undertaking the wandering alone. As a matter of fact, isolated females have been seen in various veins; but it is not sure whether they got there alone or by the help of males whom they afterwards abandoned. During this journey all females go on laying eggs—at first abnormal ones, later (i.e., after they have become impregnated), normal ones. In all wider vessels, these eggs also are taken up by the blood stream and carried back to the liver where they join those which have arrived previously. There is, however, the probability that, now, terminal-spined ones may be among them; observation tells us that indeed these occur in the liver, though in numbers which vary considerably in the individual cases. But from what has been said above we may derive as the general rule that the lateral-spined eggs will prevail, the longer the females had to wait for fertilization, whereas the terminal-spined eggs will prevail, the sooner the females became fertilized.

In the walls of bladder and rectum the worms make their way into the finer ramifications the diameter of which gradually becomes equal or even less than that of the male. From this point onwards it is difficult for the eggs laid by the female to escape into the general circulation. Pictures I have seen in sections of the vesical and rectal wall even seem to indicate that the females can stretch their (already thin) bodies to such an extent, escaping at the same time more or less from the gynaecophoric canal of the male, that their heads (close to which the genital aperture is situated) reach very fine capillaries. Eggs deposited there—either singly or in groups—would be kept in place by the walls of the vessels closing in upon them as soon as the female withdraws to her original place. The process may be repeated more or less often, a whole area becoming thus stuffed with ova. I have not seen the process here described actually going on; it is also probable that many variations occur; but the chief details are based on observed facts.

The eggs, though originally deposited in the blood vessels, finally appear in the urine or the faeces: they must have passed through the tissues of the organs. I do not consider it as illogical to admit that what happens to the eggs in the walls of bladder and rectum may also happen to the eggs in the liver. Observation actually shows them in the tissue of the organ: they, therefore, have left the blood vessels as they have in the pelvic organs. Admitting that they change their place in the tissue one will easily see that several things may happen. I will at this place only mention the possibility of some eggs getting into a blood vessel of the hepatic system. Should this take place the blood stream would carry them away from the liver; the next place where they are likely to become arrested again is the lung. Observation has shown that the organ in which, next to the liver, lateral-spined eggs are most commonly found is the lung. What happened in the liver may happen in the lung; the eggs escaping from the latter would be carried by the arterial circulation to every possible organ. As a matter of fact, stray lateral-spined eggs have been seen at very different places. I will add that the way just described is not the only one by which they may reach the lung and other organs; however, these details may here be omitted as having no direct bearing on the questions under discussion.

Returning to the eggs in the liver, there is, in addition to the possibility above mentioned, the other possibility of their getting into a part of the biliary system. In this case they would be carried to the gall bladder and thence into the intestine, from which they would be voided with the faeces. After I had ascertained that in certain cases lateral-spined eggs could not possibly be derived from rectal lesions, I came to think of this possibility as an explanation of their presence in the faeces. Observation showed that the theory held good in this case also. In the first body available the first preparation made of the bile from the bladder revealed under the microscope four lateral-spined eggs; others were found in scrapings of the bladder wall, in the bile duct and all along the intestine. Three other cases examined subsequently presented similar conditions; I have not deemed it necessary to examine more. The theory had led to a conclusion which when tested by observation proved to be correct.

This is one explanation I have to offer for the occurrence of the lateral-spined eggs in the faeces. There are others still, but I will not allow myself to enter upon details which have no direct bearing upon the question which here interests us. Observation has thus shown that the occurrence of lateral-spined eggs in the faeces of living patients is not by any means a proof of the infection of the intestine proper, and quite especially of the rectum. These eggs may, and in many cases do, come from the liver; the only question of importance which remains to be answered in this connection is the question as to the reasons, why the infection of the liver is, in certain localities as the exception, in other localities as the rule, not followed by an infection of the bladder. I will show later that there is a possibility—and to my mind not even a very far-fetched possibility—to explain this curious difference, without the help of a mythical 'new species.'

We have seen above that the 'specific pathogenic action' assigned by Dr. SAMBON to his *Sch. mansoni* does not exist, for *Sch. hæmatobium* is capable of producing the same lesions. We see now that there is no 'special anatomical habitat' either, for the lateral-spined eggs appearing in the faeces of living persons may be such of young *Sch. hæmatobium* deposited in, and voided from, the liver. It may be added that up to the present nobody appears to have seen lateral-spined eggs in females imbedded in the gynaecophoric canal of the male, and the latter imbedded in a vein of the rectal wall. I have myself seen in situ quite a number of such females, but they only contained terminal-spined ova. I do not attribute any demonstrative value to these statements, but may point out that Dr. SAMBON's theory would find an important support if he, or somebody else, could produce females collected under the conditions above mentioned, which possessed in her uterus exclusively, and as many lateral-spined eggs as the ordinary females possess terminal-spined eggs under the same conditions. I have in some instances counted the eggs in females collected from the mesenterial, rectal, and vesical veins, and have found them to vary in number between 80 and 150.*

We now come to Dr. SAMBON's third proof, the 'peculiar geographical distribution' of *Sch. mansoni*. I may freely confess

* In a case quite recently examined I found a little colony of worms in the haemorrhoidal vein, about 7 cm. distant from the anus. There were five couples and two bachelor males. All males measure (after preservation) 5-6 mm. in length; their testicles do not yet contain free spermatozoa. The females average 7 mm. in length. Their internal genital organs do not show spermatozoa. Three are also entirely free from eggs; the two others contain each one lateral-spined ovum in the ootype, none in the uterus. This observation shows that the worms may leave the liver before sexual maturity is attained, but otherwise agrees with the theory. (Note added while reading the proofs.)

that when I first read the author's own statements the statistical observations indeed seemed to strongly favour his view. However, on testing the evidence somewhat more seriously, I find that matters change their aspect considerably. Unfortunately, a number of the papers on which the evidence is based are not actually within my reach, and cannot, therefore, be compared. From those I possess I see that Dr. SAMBON quotes the literature in a rather unusual manner.

Beginning with the West Indies it is true that according to the report by Dr. HOLCOMB (1907), rectal Bilharziosis is very common in those parts and vesical infection is rare. That the latter is actually a b s e n t cannot be said, for HOLCOMB enumerates four cases (one in a man from Guatemala, two in persons from Panama and one in a Porto Rican) in which the urine c o n t a i n e d the terminal-spined ova, in one case even combined with the presence of lateral-spined ova in the faeces. Dr. SAMBON does not mention these cases, but only says that 'endemic haematuria' is not known in the West Indies. HOLCOMB states that he was not informed where, in the four cases, the infection was obtained. Since it should not have been difficult to find out whether the infected persons had been to Africa, one may I think reasonably assume that the infection was acquired in loco. At any rate, there is no proof that it was n o t of local origin. However, I will not place great weight on these cases, owing to the fact that the place of infection is, though fairly clear, yet not positively ascertained. I consider it as m o r e important that Dr. HOLCOMB has recently himself observed a case of urinary bilharziosis (information by letter). The m o s t important case is that contracted at Martinique and very carefully studied by LETULLE (1905). LETULLE did not yet know of *Sch. mansoni* and the specific pathogenic action attributed to it. But he emphatically states that he found the bladder entirely free from infection. In the intestinal lesions, the lateral-spined eggs of '*Sch. mansoni*' were seen in c o m p a n y with the terminal-spined eggs of *Sch. hæmatobium*. The dimensions of all of them, by the way, agree very well with those of *Sch. hæmatobium*, if one remembers the fact that the latter increase considerably in „size during their embryonic development. Dr. SAMBON mentions LETULLE's case as one of 'MANSON's Bilharziosis' (p. 32), but he does n o t mention that in this case (it is, so far as I am aware, the first case of 'MANSON's Bilharziosis' thoroughly studied from a pathological point of view) b o t h forms of eggs were found.

Passing now to Africa, *Sch. hæmatobium* is, according to Dr. SAMBON, alone present in Cape Colony. He refers to HARLEY's observations and quotes from this author's article: 'In all my own cases I can positively say that only one form of egg has existed, namely, that with a terminal spine. Variation in the size, length, and outline of the egg is often observable, but I have never seen any egg with even a tendency to the formation of a side spine. I even doubt whether this peculiar form exists in the *Distomum hæmatobium* itself.' I have unfortunately no access to HARLEY's paper, but LEUCKHART also mentions it, and he says: 'Restricted exclusively to the possibility of examining the urine of his patients HARLEY had no knowledge of the existence of the eggs with lateral spines, and, therefore, considered the worms as a species different from that of Egypt' (p. 507). It is thus true that HARLEY observed terminal-spined eggs only, but, unless LEUCKART's remark is incorrect (for which assumption there is not the slighest reason), simply because he h a d n o o c c a s i o n to examine faeces in which the lateral spines are found. Dr. SAMBON then refers to the observations of BROCK, and quotes: 'that BROCK and others stated that they had never encountered the egg with the lateral spine.' But, here again, BROCK himself says (p. 6): 'I have only been able to study the ova as they appear in the urine of patients suffering from Bilharzia.' I will not ask how it is possible that Dr. SAMBON makes such misleading statements in an article which apparently claims to be taken seriously. For there is no doubt that the observations of HARLEY and BROCK are anything but demonstrative of the a b s e n c e of lateral-spined eggs in South Africa, as Dr. SAMBON makes it appear by his quotations. As to the observations made in the Congo Free State, I am sorry that I have no access to the original article, and, therefore, cannot say how far its contents correspond to the summary given by SAMBON. In the discussion Dr. LOW states that in Uganda he saw exclusively rectal cases, but often also terminal-spined eggs 'in the rectum' (1907, p. 45).

Looking at this geographical evidence, as it now appears, the observer will first be struck by the fact that it has entirely lost its original neatness. The statements, mostly based on clinical observations during the daily routine work, seem contradictory, and nowhere is there a sharp line of demarcation left. I, for one, cannot see any trace of a 'peculiar geographical distribution' of the two shapes of the egg which are said to be distinctive of the alleged two species—admitting even that the statistics are all equally reliable, i.e., made with special regard to the question at issue. But, be that as it may; there is certainly no doubt about the evidence supplied by the case of LETULLE. This was, according to Dr. SAMBON's own words, a case of 'MANSON's Bilharziosis,' and, so far as I can judge, one absolutely typical both as regards the origin (Martinique) and the clinical and pathological aspects. Nevertheless, a careful study of the lesions revealed the presence in them of b o t h forms of eggs. After SAMBON, it would thus have been a 'combined' infection with *Sch. mansoni* and *Sch. hæmatobium*; an infection, however, in which *Sch. hæmatobium* did not produce i t s o w n lesions, but those of '*Sch. mansoni*.' It remains for Dr. SAMBON to show the way out of this labyrinth. For me there is no difficulty, for I say that both forms of eggs belong to the same species, and that the apparent differences between vesical and rectal Bilharziosis are not due to a difference in the species of the parasite, but to reasons which must be looked for elsewhere; we shall see later what they may be. If I were to make a 'prophecy' I would say that in a l m o s t all cases of 'MANSON's Bilharziosis,' if they are so thoroughly examined as the Martinique case was by LETULLE, the eggs of *Sch. hæmatobium* w i l l be found among the eggs of '*Sch. mansoni*.' (I have just emphasized the word 'almost'; we shall see later that there are certain conditions under which the lateral-spined ought to be present q u i t e alone). I especially recommend for examination the liver. It is a pity that it was not studied in LETULLE's case; but I can easily comprehend that there was for LETULLE no visible reason to look for ova there.

If we now compare the various pictures offered by Bilharziosis according to observers with those known from Egypt, there is no difference left except one, and this, as I must frankly confess, is a very striking one, namely, the a p p a r e n t i r r e g u l a r i t y i n t h e l o c a l i s a t i o n o f t h e l e s i o n s. In order to make my case complete I will try to show that the biology, such as I interpret it, of *Sch. hæmatobium* is perfectly sufficient to throw light on this difference also.

Before advancing any further, and in order to avoid any misunderstandings, I will repeat that I do not ignore that what I have said with regard to the nature of the lateral-spined eggs, and what I am going to say hereafter with regard to the differences in the clinical aspect of the disease, is a 'theory,' inasmuch as it has not yet been established by experimental proof. In the absence of such proof, the only thing the scientific man, desirous of advancing our knowledge, can do, is to collect carefully as many isolated facts as may be obtainable; to separate those which are (presumably) essential from those which are (presumably) accidental, and to piece all of them together into a continuous train of events. This is what I have been endeavouring to do; I cannot imagine that a theory thus built up can be wrong in its fundamentals. It must, of course, be incomplete, or may be erroneous in details. I have already pointed out that Bilharziosis, in its varying aspects, presents a peculiarly complex problem, both as regards its pathogeny and the biology of the parasite. I do not think that I am wrong when I say that the latter represents the basis of the former, especially so far as the development and the behaviour of the worm within the human body are concerned. When, with regard to this part, I have knowledge of a good number of details, I owe that to the kind collaboration of my colleagues of the Medical School and the Kasr el Aini Hospital, Dr. ELLIOT SMITH, the Anatomist, Drs. SYMMERS (now of Queen's College, Belfast) and FERGUSON, Pathologists, Dr. MADDEN and Mr. FR. MILTON, Surgeons, who have discussed with me the observations they had occasion to make during their professional work, and have given me many a valuable hint as to details with which I am less familiar. A priori, the various observations might have been explained in various ways, but the right explanation could only be one which fitted in with the biology of the parasite. *Sch. hæmatobium* has thus far successfully resisted all attempts at revealing the secret of its development. Nevertheless, we know a number of facts which definitely settle certain details; as to others, all we can do at present is to accept what seems to be most probable. For me, everything is probable as soon as it has been demonstrated in the nearest natural relatives of the *Sch. hæmatobium*, i.e., either in other Schistosomes, or in the digenetic Trematodes. I have acted according to this principle in formulating my theory. As a matter of course, in doing this, I depend upon our present knowledge. It often happens that a theory which seems probable and natural at one time is at another upset by new facts which, though not annihilating the older facts, yet make them appear in a different light. I cannot foretell at present what facts may be in store for us with regard to Bilharziosis, and, therefore, cannot say that the theory which I defend at present is t h e right one in every detail. But I think that I c a n claim that it is based upon a large number of anatomo-pathological and helminthological facts deliberately weighed and compared. I have thought these remarks necessary in the face of Dr. SAMBON's allusion that myself, and all the other workers in Egypt, have not been able within long years to find the solution of a problem which according to him was easy enough after all.

So as to be quite impersonal I will myself draw attention to an important biological point which I am not yet able to sufficiently account for. I am convinced that the lateral-spined eggs are abnormal and, probably, unfertilized. Nevertheless, when they appear in the faeces they very often contain a fully-developed miracidium. If we suppose, with some earlier authors, that mature females are, under certain circumstances, s t i l l capable of producing such lateral-spined eggs, the dilemma would resolve itself into the question as to w h a t these conditions are (spontaneous contraction; pressure of the surrounding organs, either accidental or owing to their movements; &c.). I have already said that this point is not yet determined. To me it seems, on the whole, v e r y l i t t l e p r o b a b l e, that fully mature females continue to produce lateral-spined eggs. If this be true, the presence of the miracidia would forcibly indicate that the eggs are capable of developing by parthenogenesis. From what has been observed in the hermaphroditic Trematodes it appears that the eggs m u s t be fertilized, in order to develop. A priori, one ought to expect the same also in the Trematodes with separate sexes. However, considering the unmistakable disadvantages connected with this separation in regard to the preservation of the race under the peculiar circumstances under which the Schistosomes are living, and considering further the very complicated development of many Trematodes, in which often several sexual generations occur before the sexual stage is again reached, I would hesitate to pronounce a hasty conclusion. At any rate, the presence of fully developed miracidia in lateral-spined eggs is a point which still requires to be cleared up biologically. For the question as to the specific nature of the lateral-spined ovum the point is of no consequence; for its combined presence in the same individual with the terminal-spined egg is evidence enough that only individual conditions can be responsible for its formation.

I will now try to show that the strange and striking difference offered by the clinical and pathological pictures of Bilharziosis in various places is not incapable of explanation if we consider the presumptive life history of the parasite, in connection with the habits of the host and the conditions of the country. In order to make this clear I must start from the beginning.

The miracidium (often inappropriately called 'embryo') contains in its abdominal cavity the so called 'germinal cells,' the significance and ultimate fate of which are well known from their comparative study in various other Trematodes. The existence of these cells in the Bilharzia miracidium is absolute evidence that the miracidium cannot develop directly into an adult worm, but must pass through the stage of the 'sporocyst' which, in its turn, produces, either (and probably) at once, or by one or more intermediate generations, the definite worms. All attempts made by former authors to discover an intermediary host in which this development is gone through, have failed, and so have my own efforts. I have examined hundreds of specimens of all the molluscs common in the Nile valley, without finding any sporocyst which might have been brought into relation with the Bilharzia worms. I have placed quantities of free swimming miracidia in contact with the same molluscs, without obtaining an infection. It is easy to infect molluscs with miracidia of species which actually develop in them. I will not enter into details, but only say that the Bilharzia miracidia were never seen to take any notice of any mollusc in their neighbourhood, whereas others developing in a certain mollusc soon begin to swarm about it, and may, under the microscope, even be observed to enter into it. The same negative results were obtained with larvae of insects, with fishes, and with plants. I am thus forced to the conviction that Man himself acts as intermediary host.

If this conclusion is correct it leads to the important consequence that the spread of the *Sch. hæmatobium* is not limited by the natural geographical distribution of a special intermediary host. It can spread wherever man carries it, so long as, and in so far as, the climatic and hydrographic conditions are favourable for its development. With regard to this point, I entirely disagree with Sir PATRICK MANSON who says (1907, p. 653) that the peculiar geographical limitations of *Sch. hæmatobium* are difficult to explain if it does not require the services of an intermediary host. However, I also hold that *Sch. hæmatobium* is by no means geographically so limited as it appears to be to the defenders of the existence of *Sch. mansoni*.

No investigator has hitherto succeeded in keeping the miracidia alive for more than 30-40 hours; in my personal experiments, the upper limit found was 28 hours. They must find some new shelter within this time. If they are destined to return into man directly, two possibilities are, a priori, imaginable, viz., that they enter by the mouth, or that they enter by the skin. I have found by experiment that hydrochloric acid diluted with water to the extent of 1 : 2000 kills them within 2-3 minutes, a solution of 1 : 1000 almost instantaneously; by exclusion I am thus led to the view that they enter by the skin. There are some other facts which may be interpreted in favour of this view; but I will not mention them here. In Man, the miracidium must develop into a sporocyst which, either directly, or indirectly, generates the Bilharzia worms.

We have already seen that the only organ of the body thus far known to harbour young, and sometimes very young, worms is the liver. I therefrom conclude that the liver is the habitat of the sporocyst, from which the worms later escape into the portal vein. A priori, one might think of the possibility that they can escape also into the hepatic veins. As a matter of fact, they have been found comparatively often in the vena cava (KARTULIS), the lung (SYMMERS), &c. If the liver is the seat of the sporocyst it is a curious coincidence (perhaps it is not a mere coincidence) that in the known intermediary hosts of other Trematodes, it is the liver which harbours the sporocysts.

At post mortems, it is not uncommon to find males alone in the portal vein. These males are often conspicuously of the same size, in other words, all of the same age. They must have been generated at about the same time; this would become comprehensible on the assumption that they are generated in one sporocyst. If one sporocyst may produce males I see no reason which forbids the assumption that the females take their origin in separate sporocysts. As females are, as a rule, found much more rarely than males, it may be admitted that male sporocysts are commoner than female.

This is the way in which, according to the facts at present available I am forced to explain the arrival of the parasites in the human body. I will now describe how I seem to see the connection between the special aspects of the disease and the habits of the population as they are observable, in the first place, in Egypt. In Egypt, Bilharziosis is very common. In the towns it is especially the children who are infected; among our students, there are always some who have, or have had, haematuria. Some of them assert emphatically that they have got it while in the country. In all of them the disease lasts for some years and then disappears. All severe cases come from the country. The Egyptian peasants usually work their fields in companies; sometimes of two or three, sometimes of several dozens; standing with their feet, and working with their hands, in the water or the mud. They often also bathe in companies in canals with slowly flowing water, pools, &c. One of them who is infected with urinary Bilharziosis, when urinating into the water, infects it with several hundreds, perhaps thousands, of eggs. In warm weather the miracidia hatch within a few minutes. They have at once the opportunity of finding a new shelter, either in the skin of the man who voided the eggs or in the legs or hands of one of his comrades working close by him. Many of the miracidia which enter the skin will not succeed in finding their way to the liver, but a few do so. These possibilities of infection are repeated every time a man urinates into the water. They are perhaps repeated every day the season of the Nile flood lasts. There is thus not only the possibility, but the extreme probability, that several miracidia attain their destination at short intervals.

The worms they give rise to in the liver are of about the same age. On this supposition, viz., that several miracidia succeed in gaining the liver at short intervals, it becomes probable that, from the beginning, there will be males and females. In this case, the females, grown up to the sexual stage will not have to wait long for fertilization. They will produce a few abnormal eggs, but are soon taken up by the males and carried to the pelvic organs. On the whole, therefore, only a comparatively restricted number of lateral-spined eggs will be deposited in the liver; they may, subsequently, be joined by larger numbers of terminal-spined.

The chief habitat of the adult worms is undoubtedly the bladder. The chief vein which leads them there is the inferior mesenteric vein. I will point out in passing, that during the journey an occasional couple, before reaching the vein named, may accidentally get into a side branch coming from some other part of the bowel. In such a case the worms would give rise to an isolated focus of infection, or a separate growth at an unusual place. Such unusually located lesions have often been observed, and are, I think, correctly explained in the way alluded to. The inferior mesenteric vein leads the worms to the haemorrhoidal plexus close to the anus, but not immediately to the bladder. In order to settle the very important anatomical point whether there is a connection, wide enough to let the worms pass, between the veins of the rectum and those of the bladder, Dr. ELLIOT SMITH has very kindly made a dissection of the respective parts. Since he proposes to return to this anatomical question in detail himself, I here limit myself to the statement that such connections exist, wide enough to allow, not one couple only, but two and perhaps even three to pass side by side. I have subsequently found the worms in veins which, to judge from their width and course, were such connecting branches between rectum and bladder.

I will not omit in this connection to recall the remarkable degree in which Trematodes are able to contract their bodies. I have under the microscope followed Cercariae entering into tadpoles and insect larvae. The actual opening they make in the skin of these 'supplementary' hosts is often so small that the worms assume the shape of an hour glass; but they get through it, evidently without difficulty. There is, therefore, every probability that male Bilharzia worms may manage to travel through vessels the ordinary diameter of which does not exceed a half or even a third of a millimetre.

There is thus no doubt that the parasites have a direct route from the portal vein to the bladder. Another very important question is why they do not remain in the veins of the rectum (or the intestine in general, which is apparently the original habitat of the Schistosomes), and how they find their way through the (comparatively) few connections between rectal and vesical veins into the latter. In order to explain this remarkable 'knowledge of anatomy' I will draw attention to some well-known facts derived from the comparative biology of other parasitic worms. The larvae of the *Filaria bancrofti*, e.g., after having been sucked up by a mosquito, leave the intestine by perforating its wall, and make their way into the thoracic muscles; the larvae of the *Filaria immitis* do the same, but seek the Malpighian tubes. The mature Ankylostoma worms do not live irregularly scattered throughout the small intestine, but chiefly accumulate in a certain region. Many Amphistomes inhabit the first stomach of their hosts (Ruminants), but the specimens found there are, according to my personal experience, never below a certain size. The young stages live, often by hundreds, in the small intestine. They have been swallowed along with the food, but do not at once settle in the stomach (which they have to traverse in order to get to the small intestine); it is not until they have reached a certain size at this provisional habitat in the small intestine that they return to the first stomach which is their definite habitat.

In all these cases the worms must be guided by something which makes them find their place of destination. I have no doubt that this something is given in the peculiar chemical composition of the organs, or the juices, at the respective places; in other words, the wanderings come under the phenomena of 'chemiotaxis.' One might suppose that the conditions in the small intestine of man are about the same throughout its total length (at least behind the entrance of the bile ducts). But the fact that the Ankylostoma worms normally settle in the anterior half only, is to my mind evidence that there must be differences which to the worms are noticeable, and lead them to select one special place in preference to any other. The fact that stray specimens may often be found more or less far away from this place, does not shake the rule; these specimens are 'the exceptions which strengthen the rule.'

Starting from these reflections I conclude that the Bilharzia worms, also, are guided in their journey by chemiotactic influences. I do not think it unreasonable to conceive that the venous blood coming from the bladder is chemically slightly different from that of the rectal veins, and that this difference, slight as it may be, exercises an attractive influence on the worms, thus 'leading' them to the bladder. It is in this connection certainly not without significance that the whole journey goes a g a i n s t the blood stream, just as the dog scents the game against the wind, but not with the wind. At any rate, the veins of the bladder seem to be those first sought by the worms, although the rectal veins are nearer and would serve their purpose (to bring the eggs to some place where they can easily reach the outer world) equally well. As a matter of fact, the other *Schistosoma* species known are chiefly inhabitants of the intestinal veins. In *Sch. hæmatobium* the first infection of previously healthy persons seems to normally concern the bladder, whereas (apparently) the rectum becomes implicated after repeated infections only. One might almost imagine that after numerous eggs have been deposited in the bladder, and the normal function of the organ has become more or less impaired, the blood loses for the worms its peculiar 'scent.' There may also be mechanical reasons which keep them in the rectal veins in larger numbers than before, &c. In this, or some similar way, the rectum would gradually become infected after the bladder. However, I do not find any reasonable objection either, to the assumption that in some cases some couples of worms might from the beginning remain and establish themselves in the veins of the rectum. Owing to the kindness of Dr. Ferguson, I have recently had the opportunity of examining several cases of 'early Bilharziosis of the bladder,' in which the most scrupulous inspection of the rectum could not detect any visible change in the normal aspect of that organ. Nevertheless, quite a number of (terminal-spined) eggs were found in the residue after a part of the rectal wall had been macerated in caustic potash.

In bladder (or rectum) the real oviposition begins; the eggs are at first scarce, but gradually increase in number. They are laid in the blood vessels but afterwards escape into the tissues and are finally voided from the body after having traversed the mucous membrane of the bladder (or rectum). We do not yet know how long it takes them to accomplish this journey, but some will reach the end of it in a comparatively short time, whereas others may not succeed even after a long time. In any case, they do not appear in the urine (or the faeces) at once. The beginning of the haematuria is quite insidious; from Egypt many cases are known where there was not even haematuria, the eggs were accidentally discovered in examinations of the urine made for other purposes.

While travelling through the tissues the eggs undergo their embryonic development. The eggs at any time visible in the uterus of the female worms invariably contain an undivided egg-cell. As the embryo develops within the egg shell, the egg itself increases in size, that with a mature miracidium inside measures, on an average, 0·13 to 0·15 by 0·04 to 0·06 mm., whereas immediately after formation in the ootype it is only 0·08 to 0·09 by 0·03 to 0·04 mm. in dimension. During the embryonic development, many embryos die. Their bodies become gradually decomposed, and afterwards replaced by calcareous masses; the eggs become 'calcified.' Their appearance in this state is known well enough, so I do not want to dwell on it. With the moment of the death of the embryo, the increase in size of the whole egg is stopped. The calcified eggs thus present the well-known variations in size; they remain small when they died early, they are larger when they died later.

Appearances I have seen in many sections of bilharzial tissues (of recent and old cases) make me believe that dead eggs are no longer capable of traversing the tissues as easily as living ones do. They will thus remain in the tissues more easily. In cases of very long standing they are often found quite alone; in other words, cases in which calcified eggs are found in the tissues, or voided with the excreta, are old cases.

The age the worms may reach is not yet known; for the sake of my argument we will assume that it be three years. Three years, therefore, after a man has become infected (and has had no occasion since to become re-infected!) adult worms will no longer be in his system. But during their three years' life the females have produced an immense quantity of eggs. Many of them have been voided during the same time, but as many, probably many more, are still in the tissues, and continue to be voided with the urine (or the faeces) for a more or less longer period. But their presence, and even the presence of a live miracidium in them, is by no means a sign that the worms which produced the eggs are still alive. I may mention in this connection that practitioners have now and again tried to relieve their patients by administering drugs with the view of killing the adult worms. Considering what has just been said, and considering the other fact that the great majority of Bilharzia patients do not come for relief before the evil is more or less far advanced, it will at once be understood that in nine cases out of ten every attempt at the worms will be too late. That the eggs voided still harbour a live and active miracidium is no proof that they must be derived from a comparatively recent infection. We know of cases which, according to our present knowledge, cannot be explained unless by the assumption that within the human body the miracidia enclosed in their egg shells are capable of retaining their vitality for many years. The fact is by no means an uncommon one among the parasitic worms; the encapsuled Trichina or the wheat-eel dried up in its grain are well-known instances of longevity, which also show its biological significance. For it is not difficult to understand that the longer an immature parasite is able to wait for its chance, the greater becomes the probability that it obtains the chance for getting under those conditions which allow it to grow to sexual maturity and propagate its race. I think that the capability of the miracidia, in the eggs which are not at once voided from the body, to remain alive for a very long time must be looked at from this same point of view.

We have so far considered (theoretically) what I should like to call the normal course of events, i.e., that which takes place in localities where it is comparatively easy for the miracidia to find a new host within a short time. Under these conditions there is every probability that the females have not long to wait for the males. They produce few abnormal ova, the liver remains almost free, but terminal-spined ova are deposited plentifully in the bladder or rectum, as the case may be. There is 'urinary Bilharziosis' characterised by the apparition of terminal-spined eggs in the urine; the same eggs may also appear in the faeces, but lateral-spined ones will be so scarce that they seem to be altogether absent. We will now consider what is likely to happen under conditions which are no longer so favourable to the worms.

A man, for instance, does not work, or bathe, in the water day by day, but only at intervals of weeks or months; he does not remain in the water long, but for some minutes or an hour only; he avoids the close company of others; the water itself may perhaps be quickly flowing, thus sweeping the miracidia away from the place where they have been hatched, &c., &c. Under all these conditions, combined with the short time the miracidia are able to remain alive in water, the chances of entering the skin of a new human host are considerably reduced for any which may be in the water. Many a time not one will succeed in finding him and entering his body. On a single occasion, however, a few miracidia manage to enter his skin, and one gets safely to the liver. It produces males (we know that these are much commoner than the females; the probability of picking up a male sporocyst is therefore greater). The worms grow to sexual maturity, but finding no females they wait perhaps for a certain time, and then undertake the journey to the pelvic organs alone. After some time, the liver is again free from worms; the infection, although it has taken place, remains without consequences.

The man continues exposing himself to the conditions for infection as indicated. What happened previously may be repeated at intervals, but on one of these occasions a miracidium may enter his body which produces female worms. These in due time begin to lay lateral-spined eggs. The oviposition goes on, perhaps, for a long time. The number of lateral-spined eggs increases steadily; all are carried to the liver. It is possible (I might say probable) that some of the females try to undertake their journey alone, but owing to their inferior muscular strength they may sooner or later be driven into some smaller side branch of the mesenterial, chiefly of the splenic and inferior mesenteric veins. Not one succeeds in making the entire long journey to the rectum and the bladder. Of the specimens that have left the chief track leading to these organs, one or the other may reach the wall of the large bowel, filling a small area with her lateral-spined eggs. At the end there will be a comparatively strong infection of the liver, and perhaps some isolated infected patches in the wall of the intestine, but no terminal-spined ova will ever appear, nor will there be a regular infection of the bladder. After some time the lateral-spined eggs of the liver begin to appear in the faeces, and they continue being voided in this way for several years. I have further above (p. 174) hinted at the possible existence of cases in which even the most careful post mortem examination would not detect any terminal-spined ovum in any organ; we here have the conditions under which such cases must arise. This seems to me a suitable place, too, for inserting a biological remark. I have spoken above of the presence of fully developed miricidia in lateral-spined eggs. If these eggs are unfertilized, as I hold they are, they must be capable of developing by parthenogenesis. We now see the vital advantage the parasites would derive from such a capability for the propagation of their race in localities where the conditions for infection are scarce. I may confess that from this point of view the hypothesis loses for me much of its original strangeness.

I am now able to answer the objection raised against my interpretation of the lateral-spined eggs by HOLCOMB. I suppose that the author means to say in his argument that the lateral-spined eggs could not have been derived from young females because in the course of the year during which the eggs were observed the females, though young perhaps initially, ought to have grown to sexual maturity and thus passed on to the formation of terminal-spined eggs; in other words, during a year the eggs appearing in the faeces ought to have changed from the lateral-spined to the terminal-spined type. This objection of HOLCOMB would indeed hold good if the Bilharzia eggs, like those of the intestinal parasites, were voided from the body of the host within 24 or 48 hours after their oviposition. But we know that they come from the liver, in which they have been laid by young or unfertilized females within a comparatively short period, but from which they are voided as gradually as the terminal-spined eggs are from the bladder—quite irrespective of what has in the meantime become of the worms which laid them. The observation referred to by HOLCOMB is therefore no proof against my interpretation that the lateral-spined eggs are the products of young, or unfertilized, females. It is, on the contrary, an argument in favour of it, whereas it would have been a certain evidence against my views had HOLCOMB observed that the eggs changed their shape in a marked degree in so short a period.

If we admit attempts at independent wanderings on the part of the females, it may happen that some of them, succeeding in getting near the haemorrhoidal plexus of the rectum, may find there some males, remnants of a previous infection. Or else the host may contract a new infection with another male sporocyst while some females of a previous infection are still alive in the liver. In both cases matters would assume what we have called above their normal course. After due time terminal-spined ova would appear in the urine, while the lateral-spined eggs of the liver continue being voided by way of the rectum. I will not spin out this narrative any more. I think it will now be seen that in the way alluded to the clinical and pathological picture shown by the infection in any particular individual must depend upon the more or less favourable nature of the conditions of infection to which the individual has been exposed. A first infection with one or some male sporocysts would not lead to any consequence. A first infection with a female sporocyst would give a picture typical of 'MANSON's Bilharziosis,' i.e., an untouched bladder but lateral-spined eggs appearing for years in the faeces. In all countries where infection with *Sch. hæmatobium* is possible, a man once infected will, as a rule, be subject to the opportunity of re-infection. The aspect the disease will then show must vary with the intervals at which the infection becomes repeated, and with the sex of the worms which are acquired. We may get pictures such as represented by the case of LETULLE, where the external aspect still preserved the features of 'MANSON's Bilharziosis,' but where, internally, the normal, terminal-spined eggs were found in company with the lateral-spined type. If, finally, a man once only in his life, and perhaps for a few hours only, happens to come under a peculiar combination of circumstances which favour a simultaneous entrance of a larger number of miricidia, even in a country where otherwise the conditions for infection are unfavourable, he will contract for perhaps three, perhaps six, perhaps more years 'urinary Bilharziosis,' either pure, when he was not previously infected, or mixed with 'MANSON's Bilharziosis,' when he was infected with this peculiar type before. I am personally perfectly sure that the four cases of urinary Bilharziosis quoted by HOLCOMB were contracted in loco after the fashion here described.

On the whole, therefore, I do not, from my point of view, see any sharp line of demarcation between the two types. They are simply the opposite ends of a continuous series of intermediary stages.

I cannot quit this subject without drawing attention to another point which seems to me of great interest. We have seen that LETULLE expressly states that in his case the bladder was entirely free from iufection. I can only interpret this statement in the sense that no pathological changes were perceivable in the bladder, but I cannot quite believe that a close examination would not for all that have resulted in the detection of some eggs in the tissue of the bladder. It would have been of the utmost interest to know of what type they were. Cases like LETULLE's are rare in Egypt, because of the specially favourable conditions for infection in this country. But other observers may have an easier opportunity of examining them. Instead of a tedious preparation of sections, it would suffice to macerate a piece of the bladder-wall in caustic potash, and examine the residue. The shells of the Bilharzia eggs are not at once dissolved by this reagent, and even a few eggs would be found without difficulty, if present.

The conditions unfavourable for infection as they were suggested above will in general obtain in countries where there is a thin population, where the people do not come regularly in contact with water every day for a long part of the year, where they are not in the habit of working (or bathing) in companies, where there is not much water, or where the water, though abundant, flows quickly, &c., &c. I know neither the country nor the habits of the population in South Africa, in Uganda, in the Congo Free State, or in the West Indies, but I am fairly sure that on close observation of details the special aspect of the disease will be found to vary in accordance with the conditions for infection as they have been specified above.

I have previously alluded to the relative value of statistical observations. I can now illustrate what has been said there by an instructive example. HOLCOMB (who believes in '*Sch. mansoni*') after having given an extensive account of the cases of intestinal Bilharziosis observed in tropical America, compares them with the statistics published by various observers on the relative frequency of the different forms of Egyptian Bilharziosis (1907, p. 59). The main result he comes to is that, because there is in Cairo on an average one case of intestinal to 17 cases of vesical Bilharziosis, one ought to expect the same for the West Indies, if the cause of the disease were the same parasite in both countries. The actual observations, however, show the contrary: the intestinal form is very common and the vesical form is extremely rare; therefore, it appears that in the West Indies there is also another species of parasite.

For me, the same statistics do not prove anything beyond the bare fact that the disease shows in the two countries a remarkably different aspect. In order to find out the reason for this fact, I would deem it necessary to analyse, if possible, all the factors that have, or may have, a share in bringing about the fact. The species of the parasite is one of them; the species of the host is another. But there are others, and amongst these the local conditions for infection are to my mind a factor of the first practical importance. This factor has been completely overlooked by HOLCOMB when he drew his conclusions, although its value is, so far as I have a judgment, fully recognised in modern epidemiology. Let us only assume it were possible to take one of the West Indian Islands, make its climatical and hydrographical conditions absolutely like those of Egypt, make the population (which is slightly infected with intestinal Bilharziosis) as dense as it is in the Nile Valley, make it live and work after the fashion of the Egyptian fellah, and then shut the Island off entirely from communication with the rest of the world; I have little doubt what the statistics would say some ten or twenty years hence.

Resuming now what has been said in this lengthy discussion, I must state that, of the evidence brought forward by Dr. SAMBON in order to justify the creation of '*Sch. mansoni*': 1, the zoological proof is absolutely insufficient; 2, the anatomo-pathological proof does not stand any serious test; and 3, the geographical proof is based upon a peculiarly one-sided interpretation of the literature. In all the evidence there is not the slightest detail which would really point to the existence of a distinct species in the West Indies and certain parts of Africa. It would be unwise on my part to go so far as to contend that such a species, or perhaps even several species, can not, altogether, exist. This is quite possible from the zoological point of view; but, zoologically, there is no possible doubt either that this species, or these species, must produce the same two shapes of eggs as does the *Sch. hæmatobium*, or else our present information is wholly incorrect. If, therefore, Dr. SAMBON wishes to maintain that there is an independent '*Sch. mansoni*' in the countries above-mentioned, the entire proof of its existence still remains to be given.

I cannot conclude this article without making some remarks of remonstrance with regard to another passage in Dr. SAMBON'S paper 'On the Part played by Metazoan Parasites in Tropical Pathology.' Speaking of the infection with *Agchylostoma duodenale*, he says that the theory of infection by the skin 'now stands on the firm foundation of experimental proof.' But the printed abstract (Journ. Trop. Med. 1908, p. 34) then goes on to say that 'Dr. SAMBON doubted, however, whether the trachea-oesophagus part of the journey was more than conjecture; he thought the larvae could certainly reach the intestine by a safer and more direct route.' The author then refers to the larval stages of certain Cylicostomes found encysted in the intestinal wall, and to the larvae of *Sclerostomum vulgare* living in aneurysms of the mesenteric arteries, in horses. I presume that Dr. SAMBON means to indicate by this reference that there is a connection, or an analogy, between the development of the forms mentioned and that of the Ankylostomes. If my presumption is correct, I may say in answer that thoughts of this sort are as old as they are unfounded. They will be discussed in detail in the second part of my monograph on Ankylostoma which I am at present writing. If Dr. SAMBON further 'thinks' that the larvae could 'certainly' reach the intestine by a safer and more direct route, and if he 'doubts' whether the trachea-oesophagus part of the journey is 'more than conjecture,' I cannot help it. I will only state the following facts. My actual observations concerning the wanderings of the larvae were first made known in a paper read before the Sixth International Zoological Congress at Berne in 1904. They are printed in the 'Comptes rendus' of this Congress (1905a, p. 225f.), and again described in connection with some other questions concerning Ankylostomiasis in a later paper of mine (1905b). In Berne I exhibited a series of microscopical sections showing the larvae in the different stages of their journey. These preparations afterwards went for some time to Dr. OLIVER, of Newcastle-on-Tyne, who, with my authorisation, had lantern slides of some of them made which he used in connection with a paper read by him before the North of England Institute of Mining and Mechanical Engineers (1904). Some of these photographs were afterwards (I regret to say, without my authorisation) published in SIR PATRICK MANSON'S 'Lectures on Tropical Diseases' (1905); there is one (on page 20) showing larvae in a bronchus, and another showing a larva in the larynx (on page 21; it is erroneously labelled: 'in stomach'). In 1906 I had the pleasure of presenting to the London School of Tropical Medicine a series of preparations, accompanied by a detailed description, of all the important stages of the journey of the larvae from the skin to the larynx. The tedious work of making these preparations was undertaken with the special purpose of sending them away in order to allow authors to form an individual opinion without great personal trouble, except, of course, that of looking at the preparations. Dr. SAMBON has not looked at them, nor has he consulted the literature before 'formulating his ideas.' I am sure that I do not under-estimate 'The Importance of Rational Inductive Methods in advancing Knowledge' (Journ. Trop. Med. 1908, p. 41), but I doubt whether 'ideas' like these (and several others formulated by Dr. SAMBON with regard to h e l m i n t h o l o g i c a l questions) have a right to be classed under that heading.

CAIRO, *16th March*, 1908.

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